UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. BOX 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
10/068,965	02/11/2002	Jean-Luc Balligand	DCLERC-2 P1	2383

23599 7590 08/12/2003

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1636	10

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/068,965	BALLIGAND ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-37 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-37 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).
4) ☐ Interview Summary (PTO-413) Paper No(s).
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

DETAILED ACTION

Claims 1-37 are pending in the present application, and they are subjected to the following restriction.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound is chosen from the group comprising HMGCoA reductase inhibitors, classified in class 514, subclass 423.

II. Claims 1-3, 7-8, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound is chosen from the group comprising ACAT inhibitors, can not be classified because most of the listed compounds have trademark names.

III. Claims 1-3, 9-10, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the

Fibrate [illegible] compound.

increases the export of cholesterol out of peripheral cells through the increased abundance of HDL particles resulting in the modulation of caveolin-1.

IV. Claims 1-3, 11-12, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound decreases the production of cholesterol-rich VLDL particles by the liver and is selected from the group comprising nicotinic acid, classified in class 514, subclass 546.

V. Claims 1-2, 13-14, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is recombinant caveolin-1, classified in class 514, subclass 2.

VI. Claims 1-2, 13-14, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is recombinant eNOS, classified

VII. Claims 1-2, 13-14, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is recombinant calmodulin, classified in class 514, subclass 2.

VIII. Claims 1-2, 13-14, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is recombinant Hsp90, classified in class 514, subclass 2.

IX. Claims 1-2, 13, 15, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is a nucleic acid encoding the partial or total amino acid sequence of caveolin-1 or an analogue thereof, classified in class 514, subclass 44.

X. Claims 1-2, 13, 16, 27-28, 31-37, drawn to a compound for use as a

compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is a nucleic acid encoding the partial or total amino acid sequence of e-NOS or an analogue thereof, classified in class 514, subclass 44.

XI. Claims 1-2, 13, 17-19, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an antisense nucleic acid able to hybridise with a corresponding nucleotide sequence encoding the caveolin-1, classified in class 514, subclass 44.

XII. Claims 1-2, 13, 20, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an antagonist of caveolin-1, can not be classified because the structure of the antagonist is not recited.

XIII. Claims 1-2, 13, 20, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the

Hsp90 or calmodulin and the compound is an antagonist of eNOS, can not be classified because the structure of the antagonist is not recited.

XIV. Claims 1-2, 13, 20, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an antagonist of calmodulin, can not be classified because the structure of the antagonist is not recited.

XV. Claims 1-2, 13, 20, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an antagonist of Hsp90, can not be classified because the structure of the antagonist is not recited.

XVI. Claims 1-2, 13, 20, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an agonist of caveolin-1, can not be classified because the structure of the agonist is not recited.

intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an agonist of eNOS, classified can not be classified because the structure of the agonist is not recited.

XVIII. Claims 1-2, 13, 20, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an agonist of calmodulin, can not be classified because the structure of the agonist is not recited.

XIX. Claims 1-2, 13, 20, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is an agonist of Hsp90, can not be classified because the structure of the agonist is not recited.

XX. Claims 1-2, 13, 21, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS,

caveolin-1 preventing its binding to the eNOS, can not be classified because the structure of the compound is not recited.

XXI. Claims 1-2, 13, 22, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is a nucleic acid encoding the partial or total amino acid sequence of eNOS or the eNOS sequence deleted or mutated in the active caveolin binding site or an analogue thereof, classified in class 514, subclass 44.

XXII. Claims 1-2, 13, 23, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is a trapping molecule comprises an amino acid sequence of SEQ ID NO:4, SEQ ID NO:6 to SEQ ID NO:86, classified in class 514, subclass 2. It is noted that claim 23 is improperly dependent on claim 22.

XXIII. Claims 1-2, 13, 24-25, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the [illegible] wherein the compound influences abundance and/or [illegible]

Hsp90 or calmodulin and the compound is able to trap the endogenous eNOS preventing the formation of NO and the compound is an amino acid sequence comprises SEQ ID NO:2 and/or SEQ ID NO:3, classified in class , subclass .

XXIV. Claims 1-2, 13, 24, 26, 27-28, 31-37, drawn to a compound for use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway, wherein the compound influences abundance and/or activity of calveolin-1, eNOS, Hsp90 or calmodulin and the compound is able to trap the endogenous eNOS preventing the formation of NO and the compound is a nucleotide sequence encoding the partial or total amino acid sequence of caveolin or an analogue, classified in class 514, subclass 44.

XXV. Claim 29, drawn to a diagnostic kit for the testing of a compound or a composition for their ability to modulate angiogenesis via the intracellular free cholesterol-caveonlin1-eNOS-NO pathway can not be classified because the claim does not recite any component in the diagnostic kit.

XXVI. Claim 30, drawn to a method for screening compounds or compositions which modulate angiogenesis via the intracellular free cholesterol-caveonlin1-eNOS-NO pathway can not be classified because the claim does not recite any method step.

medicament for the modulation of angiogenesis though the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway comprises distinct compounds that are chemically distinct, without substantial common structures among themselves and that they function via different mechanisms for attaining the desired results contemplated by Applicants. These compounds include: (1) HMGCoA reductase inhibitors (Group I); (2) ACAT inhibitors (Group II); (3) fenofirate, benzafibrate and ciprofibrate (Group III); (4) nicotinic acid (Group IV); (5) recombinant aveolin-1 (Group V); (6) recombinant eNOS (Group VI); (7) recombinant calmodulin (Group VII); (8) recombinant Hsp90 (Group VIII); (9) nucleic acid encoding partial or total amino acid sequence of caveolin-1 (Group IX); (10) nucleic acid encoding partial or total amino acid sequence of e-NOS (Group X); (11) an antisense nucleic acid of caveolin-1 (Group XI); (12) an antagonist of caveolin-1 without known structure (Group XII); (13) an antagonist of eNOS without known structure (Group XIII); (14) an antagonist of calmodulin without known structure (Group XIV); (15) an antagonist of Hsp90 without known structure (Group XV); (16) an agonist of caveolin-1 without known structure (Group XVI); (17) an agonist of eNOS without known structure (Group XVII); (18) an agonist of calmodulin without known structure (Group XVIII); (19) an agonist of Hsp90 without known structure (Group XIX); (20) a compound without known structure having the ability to trap the endogenous caveolin-1 (Group XX); (21) a nucleic acid encoding partial or total amino acid sequence of eNOS deleted or mutated in the active caveolin binding site (Group XXI); (22)

(24) a nucleotide encoding the partial or total amino acid sequence of caveolin that is able to trap endogenous eNOS. The methods of using these distinct compounds have different starting materials, different method steps (route of administration and dosage depending which compounds are utilized) and that they require different technical consideration for attaining the desired end-results. Therefore, the inventions of Groups I-XXIV are capable of supporting separate patents. **Additionally**, as set forth in MPEP 803.02, unity of invention exists if all species recited in a claim (1) shows a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Additionally, should Applicants elect the invention of Group XXII, claims 1-2, 13, 23, 27-28, 31-37 link patentably distinct inventions that lack the unity of invention. This is because compounds and their use as a medicament for the modulation of angiogenesis through the tackling of the intracellular free cholesterol-caveolin1-eNOS-NO pathway comprising amino acid sequences of SEQ ID NO:4, SEQ ID NO:6 to SEQ ID NO:86 that are distinct, and that they are not necessarily have the same desired activity as a trapping molecule. As set forth in MPEP 803.02, unity of invention exists if all species recited in a claim (1) shows a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. Furthermore, a search of more than one of the listed SEQ ID NOs presents an undue burden on the Patent and Trademark Office. Applicant is required to elect a specific SEQ ID NO.

including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-132(CCPA 1971). See also MPEP 804.01.

The inventions are distinct, each from the other because of the following reasons:

Inventions I to XXIV are drawn to distinct compounds and their uses for the reasons already set forth in the preceding paragraphs.

The diagnostic kit for testing a compound or a composition for the ability to modulate angiogenesis of Group XXV does not require any of the compounds of Groups I to XXIV, nor it is required for the screening method of Group XXVI.

The method of screening compounds or compositions which modulate angiogenesis of Group XXVI does not require any compounds in Groups I to XXIV, and it is a distinct and independent method from the use of the same compounds as medicaments.

Because these inventions are distinct for the reasons given above and have

[illegible] [illegible] [illegible] [illegible] [illegible] [illegible]

different literature searches), it would be unduly burdensome for the examiner to search and/or consider the patentability of all the inventions in a single application. Therefore, restriction for examination purposes as indicated is proper.

A telephone call was made to Mr. Anthony J. Zelano on August 4, 2003 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17 (h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

Quang Nguyen, Ph.D.